The US Select Agent Rule and an International Opportunity to Achieve Defensible Biosecurity Guidelines

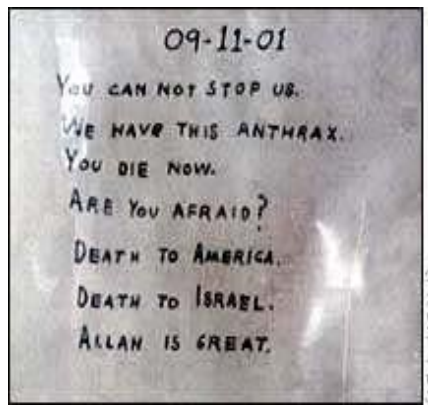
2004 Asia Regional Workshop:
The Future of the Biotechnology Industry
Singapore
April 27, 2004

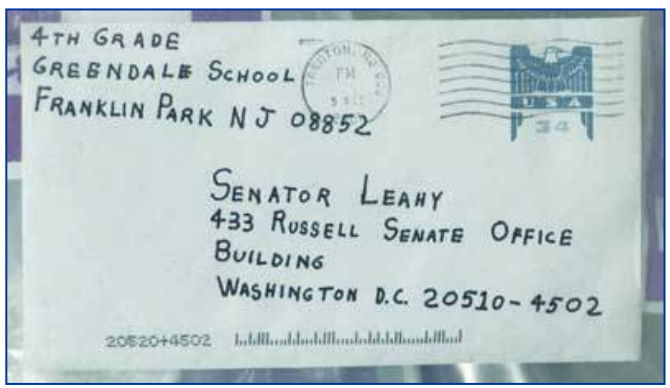
Reynolds M. Salerno, Ph.D.
Sandia National Laboratories

SAND No. 2004-1630C

Bioterrorist and Biological Weapons Threat

- Increase in awareness of bioterrorist and biological weapons threat in the US
- Emerging US security regime: policies with two sets of objectives
  - Enhance ability to respond to public and agricultural health emergencies
  - Reduce the risk that bioscience and biotechnology could be used maliciously
- Focus of this talk is biosecurity: protection of certain biological materials at bioscience facilities from theft and sabotage



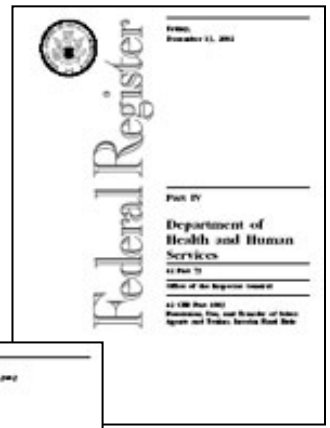


Problem: Bioscience Research and International Security

- Recent realization that bioscience facilities are potential sources of viable and virulent pathogens and toxins
  - Bioscience community not accustomed to security
- New US regulatory environment has broad international repercussions
  - International community must address this issue
- Control of certain biological materials is necessary
  - But *how* that is achieved must be carefully considered and implemented

New US Regulatory Environment for Biosecurity

- USA PATRIOT Act of 2001 – US Public Law 107-55
  - Restricted Persons
- Bioterrorism Preparedness Act of 2002 – US Public Law 107-188
  - 42 CFR 73 (Human)
  - 9 CFR 121 (Animal)
  - 7 CFR 331 (Plant)
- The CFR require specific measures
  - Registration of a facility if they possess one of the 82 Select Agents
  - Background checks for individuals with access to Select Agents
  - Facility must designate a Responsible Official
  - Security, safety, and emergency response plans
  - Safety and security training
  - Regulation of transfers of Select Agents
  - Recordkeeping
  - Safety and security inspections



Human Select Agents and Toxins

- Crimean-Congo haemorrhagic fever virus
- Ebola viruses
- Cercopithecine herpesvirus 1 (Herpes B virus)
- Lassa fever virus
- Marburg virus
- Monkeypox virus
- South American Haemorrhagic Fever viruses (Junin, Machupo, Sabia, Flexal, Guanarito)
- Tick-borne encephalitis complex (flavi) viruses
- Variola major virus and Variola minor virus (Alastrim)

- *Rickettsia prowazekii*
- *Rickettsia rickettsii*
- *Yersinia pestis*
- *Coccidioides posadasii*

- Abrin
- Conotoxins
- Diacetoxyscirpenol
- Ricin
- Saxitoxin
- Tetrodotoxin
- Shiga-like ribosome inactivating proteins

Overlap Select Agents and Toxins

- Eastern equine encephalitis virus
- Nipah and Hendra complex viruses
- Rift Valley fever virus
- Venezuelan equine encephalitis virus

- Botulinum neurotoxins
- *Clostridium perfringens* epsilon toxin
- Shigatoxin
- Staphylococcal enterotoxins
- T-2 toxin

- *Bacillus anthracis*
- *Brucella abortus*
- *Brucella melitensis*
- *Brucella suis*
- *Burkholderia mallei*
- *Burkholderia pseudomallei*
- Botulinum neurotoxin producing species of *Clostridium*
- *Coxiella burnetii*
- *Francisella tularensis*

- *Coccidioides immitis*

Animal Select Agents and Toxins

- African horse sickness virus
- African swine fever virus
- Akabane virus
- Avian influenza virus (highly pathogenic)
- Bluetongue virus (exotic)
- Pox viruses (camel, goat, sheep)
- Classical swine fever virus
- Foot and Mouth Disease virus
- Japanese encephalitis virus
- Lumpy skin disease virus
- Malignant catarrhal fever virus
- Newcastle disease virus
- Peste des petits ruminants virus
- Rinderpest virus
- Swine vesicular disease virus
- Vesicular stomatitis virus (exotic)

- *Cowdria ruminantium*
- *Mycoplasma capricolum*
- *Mycoplasma mycoides*

- Bovine spongiform encephalopathy agent

Plant Select Agents and Toxins

- **Plum pox potyvirus**

- ***Liberobacter africanus***
- ***Liberobacter asiaticus***
- ***Ralstonia solanacearum***
- ***Xanthomonas oryzae***
- ***Xylella fastidiosa***

- ***Peronosclerospora philippinensis***
- ***Phakopsora pachyrhizi***
- ***Sclerophthora rayssiae***
- ***Synchtrium endobioticum***

Scientific Concerns

- Top-down security regime
- No need to acquire biological material from a bioscience facility to pursue bioterrorism
- Nature of the material makes diversion extremely difficult to prevent
- Dual-use characteristics of biological materials and technology make identification of illegitimate activities extremely difficult

REPORTS

Chemical Synthesis of Poliovirus cDNA: Generation of Infectious Virus in the Absence of Natural Template

Jeronimo Cello, Aniko V. Paul, Eckard Wimmer*

9 AUGUST 2002 VOL 297 SCIENCE www.sciencemag.org

JOURNAL OF VIROLOGY, Feb. 2001, p. 1205–1210 Vol. 75, No. 3
0022-538X/01/$04.00+0 DOI: 10.1128/JVI.75.3.1205–1210.2001

Expression of Mouse Interleukin-4 by a Recombinant Ectromelia Virus Suppresses Cytolytic Lymphocyte Responses and Overcomes Genetic Resistance to Mousepox

RONALD J. JACKSON,[1,2]* ALISTAIR J. RAMSAY,[2]† CARINA D. CHRISTENSEN,[2] SANDRA BEATON,[1] DIANA F. HALL,[1]‡ AND IAN A. RAMSHAW[2]

Pest Animal Control Cooperative Research Centre, CSIRO Sustainable Ecosystems,[1] and Division of Immunology and Cell Biology, John Curtin School of Medical Research, Australian National University,[2] Canberra, Australia

Security Concerns

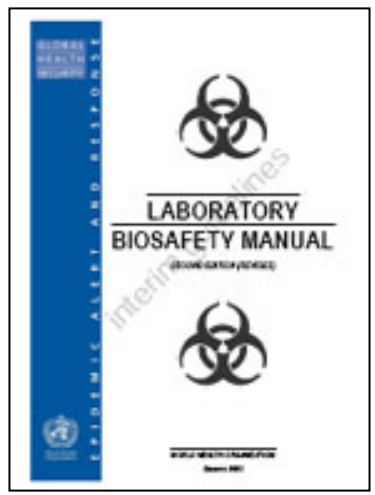
- The most likely threat to viable and virulent biological material is from someone who has legitimate access to the facility
  - Traditional facility security approaches focus on protecting against outside adversaries
- Very few agents can be easily and successfully deployed as mass-casualty weapons
  - US regulations based on 82 agents and toxins of various degrees of attractiveness to adversaries
- No protection if personnel do not understand and accept security
  - Evasion of security measures
  - Withdrawal from research on Select Agents

Achieving International Biosecurity

- "Infectious diseases make no distinctions among people and recognize no borders"
  - President George Bush, November 2001
- Securing pathogens and toxins must be an international endeavor to mitigate the threat of BW proliferation
- International regulatory regime would not be appropriate because of dual-use nature of all bioscience
- International guidelines should be promulgated by a respected technical organization in the public health field
  - World Health Organization

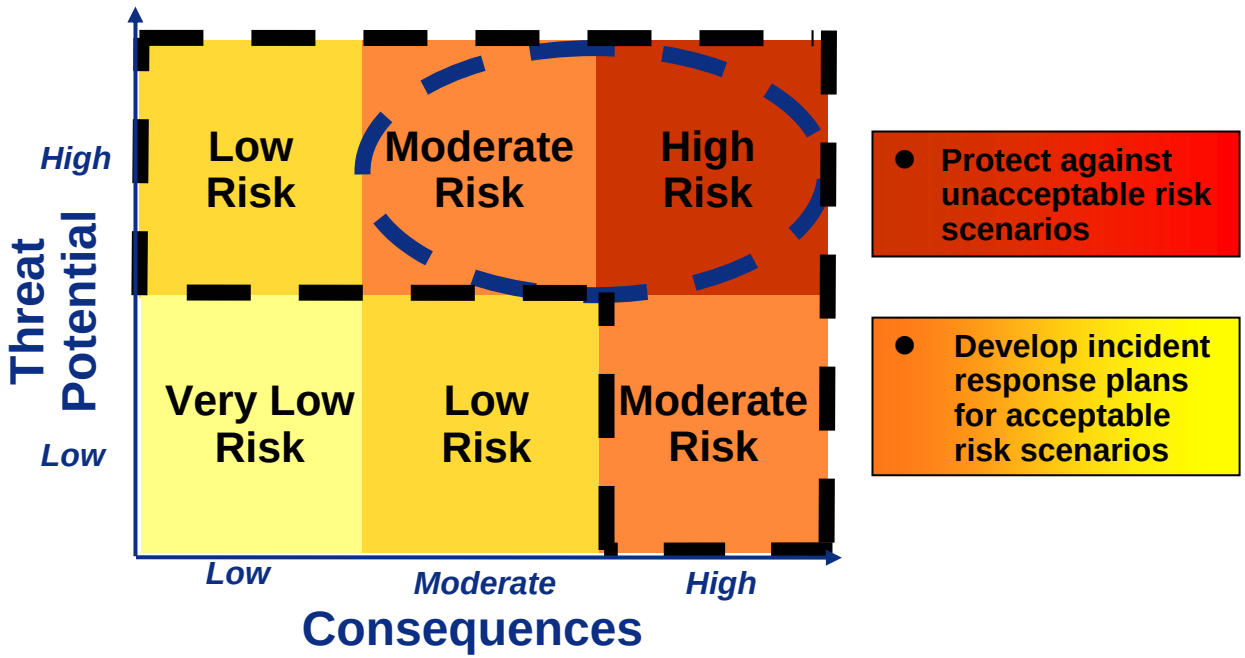
Biosafety as a Model

- Biosafety aims to reduce or eliminate accidental exposure to or release of hazardous agents
  - CDC/NIH “Biosafety in Microbiological and Biomedical Laboratories” (BMBL)
  - WHO “Laboratory Biosafety Manual” (LBM)
- Four biosafety levels
  - Graded application of practices and techniques, laboratory equipment, and facility design (“containment”)
  - Based on agent safety risk assessments
- Biosafety now considered standard microbiological practice around the world



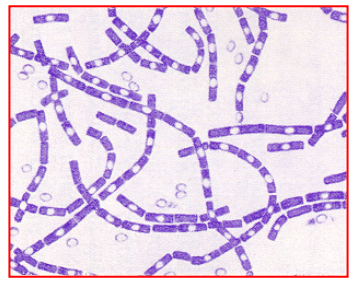
Defensible & Achievable Biosecurity Guidelines

- **Employ a risk management approach**
  - **Risk will always exist: every asset cannot be protected against every threat**
  - **Distinguish between "acceptable" and "unacceptable" risks**
- **Develop a methodology so that facilities can conduct agent-based security risk assessments**
  - **Ensures that protection for an asset, and the cost, is proportional to the risk of theft or sabotage of that asset**

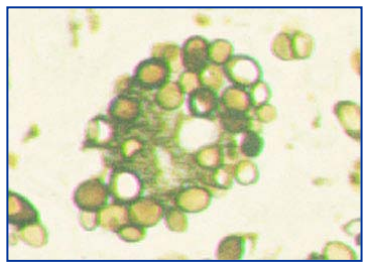


Biological Agent Security Risk Assessment

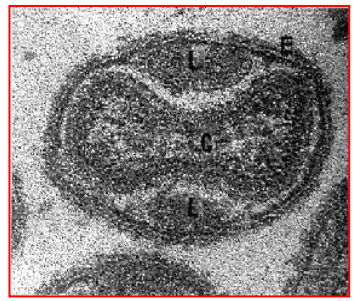
- All pathogens and toxins do not need the same level of protection
- Agents should be placed in a Biosecurity Level based upon their risk of theft and use as a biological weapon
  - Risk should be a function of both weaponization potential and consequences of use
- Weaponization potential is the ease or difficulty that an agent may be successfully deployed as a weapon
- Consequences of use are associated with the infectious disease characteristics of the agent



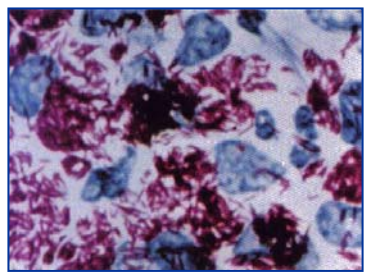
Bacillus anthracis



Coccidioides immitis



Variola major



Mycobacterium leprae

Biological Agent Security Risk Levels

- **Low Risk Pathogens and Toxins (LRPT)**
  - Relatively difficult to deploy as a weapon, and/or
  - Use as a weapon would have few consequences
- **Moderate Risk Pathogens and Toxins (MRPT)**
  - Relatively difficult to deploy as a weapon, and
  - Use as a weapon would have localized consequences with low to moderate casualties and/or economic damage
- **High Risk Pathogens and Toxins (HRPT)**
  - Not particularly difficult to deploy as a weapon, and
  - Use as a weapon could have national or international consequences, causing moderate to high casualties and/or economic damage
- **Extreme Risk Pathogens and Toxins (ERPT)**
  - Would normally be classified as HRPT, except that they are not found in nature (eradicated)
  - Could include genetically engineered agents, if they were suspected of being a HRPT

Results of a Biosecurity-Level System

- Most pathogens and toxins would likely be LRPT
- Most current Select Agents would likely be MRPT
- Security associated with LRPT and MRPT would be achievable at reasonable cost for the broad biological research community
  - Rely largely on existing biosafety measures
- Very few Select Agents would be HRPT or ERPT
- Security for facilities that work with HRPT or ERPT would be relatively significant, but should still
  - Rely largely on policies and procedures
  - Be transparent to the users
  - Use resources efficiently
  - Not unnecessarily hinder normal operations (e.g. research, diagnostics, biosafety)

Summary

- Necessary to take steps to reduce the likelihood that certain pathogens and toxins could be stolen from bioscience facilities
- Critical that these steps are designed specifically for biological materials and research
- Most biosecurity measures should reinforce and complement existing biosafety measures
- Need to involve international scientific community in development of a comprehensive approach and widely accepted model for biosecurity
  - Important to build understanding and acceptance

Contact Information

Reynolds M. Salerno, Ph.D.
Principal Member of the Technical Staff
Sandia National Laboratories
PO Box 5800, MS 1373
Albuquerque, NM 87185
USA
Tel. 505-844-8971
email: rmsaler@sandia.gov

www.biosecurity.sandia.gov